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DOI:
10.1136/thoraxjnl-2015-207697

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Document Version
Peer reviewed version

Citation for published version (Harvard):
Lugg, ST, Agostini, PJ, Tikka, T, Kerr, A, Adams, K, Bishay, E, Kalkat, MS, Steyn, RS, Rajesh, PB, Thickett, DR & Naidu, B 2016, 'Long-term impact of developing a postoperative pulmonary complication after lung surgery', *Thorax*, vol. 71, no. 2, pp. 171-176. https://doi.org/10.1136/thoraxjnl-2015-207697

Link to publication on Research at Birmingham portal

Publisher Rights Statement:
This article has been accepted for publication in Thorax, 2016 following peer review, and the Version of Record can be accessed online at: http://dx.doi.org/10.1136/thoraxjnl-2015-207697

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Long-term impact of developing a postoperative pulmonary complication after lung surgery

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Keywords Thoracic surgery, lung cancer, pneumonia, COPD pathology, tobacco and the lung.

Word Count 3070, excluding title, abstracts, references, figures and tables.

What is the key question? Does the development of a postoperative pulmonary complication (PPC) following thoracic surgery for lung resection impact on long-term survival?

What is the bottom line? After excluding immediate post-operative deaths, developing a PPC is a significant independent risk factor for late deaths and these patients have a worse long-term survival.

Why read on? We demonstrate in our large prospective cohort that PPCs are common following thoracic surgery, both the short and long-term effects of developing a PPC are striking; COPD and smoking are significant independent risk factors.

ABSTRACT

Introduction Postoperative pulmonary complications (PPC) such as atelectasis and pneumonia are common following lung resection. PPCs have a significant clinical impact on postoperative morbidity and mortality. We studied the long-term effects of PPCs and sought to identify independent risk factors.

Methods A prospective observational study involved all patients following lung resection in a regional thoracic centre over 4 years. PPCs were assessed daily in hospital using the Melbourne group scale based on chest x-ray, white cell count, fever, purulent sputum, microbiology, oxygen saturations, physician diagnosis and intensive therapy unit (ITU)/high dependency unit readmission. Follow up included hospital length of stay (LOS), 30-day readmissions, and mortality.

Results 86 of 670 patients (13%) who underwent a lung resection developed a PPC. Those patients had a significantly longer hospital LOS in days (13, 95%CI 10.5-14.9 vs. 6.3, 95%CI 5.9-6.7; p<0.001) and higher rates of both ITU admissions (28% vs. 1.9%; p<0.001) and 30-day hospital readmissions (20.7% vs. 11.9%; p<0.05). Significant independent risk factors for development of PPC were COPD and smoking (p<0.05), not age. Excluding early postoperative deaths, developing a PPC resulted a significantly reduced overall survival in months (40 95%CI 34-44 vs. 46 95%CI 44-47; p=0.006). Developing a PPC is associated with a higher non-cancer related late deaths (11 vs. 5%; p=0.020). PPC is a significant independent risk factor for late deaths in non-small cell lung cancer patients (HR 2.0, 95%CI 1.9-3.2; p=0.006).

Conclusion Developing a PPC after thoracic surgery is common and is associated with a poorer long-term outcome.

BACKGROUND

Lung cancer is the most common cause of cancer death within the UK [1]. For those patients diagnosed with non-small cell lung cancer (NSCLC) potentially curative surgery is generally accepted as the most effective treatment [2]. There is some evidence that patients with lung cancer in the UK present at a later stage and have a higher comorbidity than patients in some other European countries [3]. Thus, surgical resection rates amongst those with proven NSCLC are lower in the UK (14%) compared to central Europe (24%) [4, 5]. To address this most recent European and UK guidelines has widened the selection criteria for lung cancer surgery [6], which

has helped improve resection rates. The 5-year survival rates for lung cancer in the UK is poor (9%) compared to central Europe (13%) as demonstrated in the 1999-2007 EUROCARE-5 report [7]. A more recent study has shown that cancer survival in England is improving, however continued investment is needed to close this international gap [8]. Furthermore, whilst in hospital mortality has fallen over the last 3 decades, mortality rates within the first 90 days of surgery are considerable [9]. We need to understand the causes of these late complications if we are to improve long-term outcomes.

Lung cancer resection is also associated with a considerable risk of postoperative pulmonary complications (PPCs), of which pneumonia and atelectasis are the most common [10]. PPCs have a significant health and economic impact on patients and health care services. Indeed, as less fit patients are undergoing surgery, the incidence of PPCs is likely to increase further. The longer-term effects of developing a PPC in hospital following lung cancer surgery have not been defined. The identification of modifiable risk factors for PPCs has a crucial role in the development of innovative strategies to reduce the impact and incidence of PPCs. We hypothesise that PPCs are associated with the late postoperative mortality and morbidity observed following lung resection.

This study aims to assess both immediate and long-term impact of PPCs, and to identify potentially modifiable independent risk factors.

METHODS

This prospective observational study was conducted at a single centre large regional thoracic unit serving 6 million people. Consecutive patients who underwent open thoracotomy or video-assisted thoracoscopic surgery (VATS) for lung resection/removal in a regional thoracic centre between April 2010 and April 2014 were observed. This study was conducted with the approval of the National Research Ethics Service (NRES) Committee West Midlands. This study was registered with the Birmingham Heartlands Hospital audit department (audit code 1672). Decisions regarding patient operability and resectability were informed by the British Thoracic Society guidelines for lung cancer resection [6].

Patients were admitted to hospital on the day of surgery. All operations were performed with single lung ventilation under general anaesthesia, and patients were subsequently scheduled for extubation in the operating room. Postoperatively, patients were managed in a dedicated thoracic high dependency unit HDU (level 2) and ward unless complications required their admission to the ITU. Postoperative pain control was achieved by continuous thoracic epidural analgesia, paravertebral infusion, intrathecal morphine and/or intercostal blocks or systemic opioids (parenteral administration or intravenous patient-controlled administration). The choice of analgesic technique was made by the anaesthetist after discussion with the patient. From the first postoperative day, all patients had a daily physiotherapy programme comprising deep breathing exercises, incentive spirometry, supported coughing and mobilisation.

The Melbourne Group Scale (MGS) is a standardised scoring system validated by our group to define the presence of a PPC such as pneumonia or clinically significant

111 atelectasis, which are likely to adversely affect the patient's clinical course [10-11].
112 Using this score, PPC is defined in those patients presenting with four or more of the
113 following eight dichotomous factors: chest x-ray (CXR) findings of atelectasis or
114 consolidation; raised white cell count (WCC) (>11.2x10^9/l); temperature >38°C; signs
115 of infection on sputum microbiology; purulent sputum differing from preoperative
116 status; oxygen saturations <90% on room air; physician diagnosis of pneumonia; and
117 prolonged HDU stay or readmission to HDU or ITU for respiratory complications. The
118 MGS was used daily by senior physiotherapists who were performing their routine
119 respiratory assessments. The discharge criteria, agreed with investigators in advance
120 included patients who were medically fit and who had been discharged from
121 physiotherapy.

122 Data collected included demographics and pre-operative record of smoking status,
123 body mass index (BMI), percentage predicted forced expiratory volume in one
124 second (FEV_1), American Society of Anesthetist (ASA) score, subjective preoperative
125 activity level and comorbidities including chronic obstructive pulmonary disease
126 (COPD) defined by clinical diagnosis of the referring clinician and staged according to
127 percentage predicted FEV_1. Postoperative data included type of analgesia used and
128 underlying pathology (including lung cancer staging if applicable). Total length of
129 stay (LOS) was defined as the LOS in hospital after the date of surgery. The HDU and
130 ITU LOS were also recorded, as well as ITU admission and 30-day readmission to
131 hospital secondary to surgical or pulmonary complications. All patients were
132 followed up for overall survival (OS) and the cause of death was obtained from both
133 the death certificate and hospital records. Deaths were classified as postoperative

complication for patients who died within initial hospital admission or within 30 days of surgery, cancer related for those patients who died of disease progression/recurrence, and non-cancer related, or cause of death uncertain where records were not available or unclear.

Statistical analysis

Results are expressed as mean (SD or 95% CI) for continuous variables and as a percentage for categorical variables. Univariate analysis of risk factors for development of PPC were assessed by performing individual un-adjusted logistic regression analysis, inclusion of one covariate at a time. Risk ratios with 95%CI were generated for variables found to have statistically significant association with PPC on univariate analysis. A backward multivariate binary logistic regression analysis was performed to identify the independent predictors of PPC within this dataset.

The effect of PPC on hospital, HDU and ITU LOS were assessed using the Mann-Whitney non-parametric test to accommodate for the presence of positive skewness. Kaplan Meyer plots and the log-rank test were used to assess the impact of PPC on survival. Cox regression was assessed including all risk factors in a model for long-term survival. All analyses were performed using the IBM SPSS version 20 and SAS 9.3 statistical package version (SAS Institue, Inc, Carry NC).

RESULTS

There were 670 patients who underwent pulmonary resections during the study period; 377 of who were male (56%). The mean±SD age of the group was 66.4±10.8

years. Mean predicted FEV_1 was 80.2±20.8%, mean BMI 26.9±8.1 kg/m^2, 328 patients (49%) had an ASA score ≥3, 176 patients (26%) had COPD, 149 patients (22%) were current smokers.

The most frequent procedure was lobectomy (n=497, 74%) followed by wedge or segmentectomy (n=111, 16%) and pneumonectomy (n=37, 5.5%). VATS lobectomy and segmentectomy were also performed (n=54, 8% and n=8, 1% respectively). Most common histological diagnosis was NSCLC (n=477, 71.2%) followed by benign disease (n=73, 11%) and metastatic disease of non-lung primary (n=69, 10.3%). Eighty-eight patients (13%) had clinical evidence of PPC using the MGS. The median day of this occurring was day 2 postoperative. The four most common positive factors to trigger a score of 4 were raised WCC (n=75, 85%), purulent sputum (n=72, 82%), CXR findings (n=69, 78%) and reduced saturations (n=68, 77%).

On univariate analysis (table 1) the significant risk factors associated with developing a PPC were percentage predicted FEV_1, ASA >3 (Risk Ratio [RR] [4 vs. 1] 4.11, 95%CI 1.53-11), self-reported preoperative activity level ≤400m (RR 1.8, 95%CI 1.20-1.68), COPD diagnosis (RR 2.13, 95%CI 2.45-15.01) and current smoking (RR [current vs. never] 6.06, 95%CI 2.57-3.40) ($p<0.05$). Age, BMI, type of surgery (individually or collectively), VATS approach, cancer diagnosis or staging and cardiovascular disease was not significantly associated with development of PPC.

Table 1 Baseline characteristics in PPC and non-PPC groups including univariate analysis of risk factors associated with developing PPC.

Variables	**Value**	**Total (n=670)**	**PPC (n=88)**	**Non-PPC (n=582)**	**P-value**
Age	Mean (±SD)	66.4 (±10.8)	67.1 (±9.6)	66.4 (±11)	0.547
FEV_1% predicted	Mean (±SD)	80.2 (±20.8)	75.8 (±20.7)	80.94 (±20.7)	0.034
BMI	Mean (±SD)	26.9 (±8.1)	27.2 (±5.6)	26.9 (±8.4)	0.757
Gender	Male Female	377 (66%) 293 (44%)	57 (65%) 31 (35%)	320 (55%) 262 (45%)	0.086
ASA Score	1 2 3 4	44 (7%) 298 (44%) 313 (47%) 15 (2%)	5 (6%) 32 (36%) 44 (50%) 7 (8%)	39 (7%) 266 (46%) 269 (46%) 8 (1%)	0.004
Pre-operative activity level	≤ 400 m > 400 m	185 (27%) 465 (73%)	35 (42%) 49 (58%)	150 (27%) 416 (73%)	0.005
Type of surgery	Lobectomy Subsegmentectomy/wedge Pneumonectomy Exploratory/biopsy Sleeve Chest wall	497 (74%) 111 (16%) 37 (6%) 13 (2%) 8 (1%) 4 (1%)	64 (73%) 15 (17%) 3 (3.5%) 3 (3.5%) 2 (2%) 1 (1%)	433 (74%) 96 (16.5%) 34 (6%) 10 (2%) 6 (1%) 3 (0.5%)	0.651
VATS	Yes No	62 (9%) 608 (91%)	9 (10%) 79 (90%)	53 (9%) 529 (91%)	0.735
Analgesia	Epidural Intrathecal morphine	254 (38%) 146 (22%)	27 (31%) 23 (26%)	227 (39.4%) 123 (21.4%)	0.443

	Morphine Infusion PCA Paraveterbral Other	63 (9.5%) 50 (7.5%) 146 (22%) 5 (1%)	9 (10%) 4 (5%) 24 (27%) 1 (1%)	54 (9.3%) 46 (8%) 122 (21.2%) 4 (0.7%)	
Pathology	NSCLC Small cell LC Carcinoid Metastatic disease Benign Other	477 (71.2%) 10 (1.5%) 27 (4%) 69 (10.3%) 73 (11%) 14 (2%)	64 (73%) 3 (3%) 4 (4.5%) 6 (7%) 11 (12.5%) 0	413 (71%) 7 (1%) 23 (2%) 63 (11%) 62 (11%) 14 (4%)	0.598
NSCLC Staging	0 IA IB IIA IIB IIIA IIIB IV	5 (1%) 120 (26%) 112(24%) 94 (20%) 53 (11%) 77 (16%) 5 (1%) 4 (1%)	0 13 (22%) 10 (17%) 14 (23.3%) 9 (15%) 13 (22%) 0 1 (1.7%)	5 (1%) 107 (26%) 102 (25%) 80 (20%) 44 (11%) 64 (16%) 5 (1.3%) 3 (0.7%)	0.762
COPD	Yes No	176 (26%) 494 (74%)	38 (43%) 50 (57%)	138 (24%) 444 (76%)	<0.001
COPD Severity (FEV_1% predicted)	Mild (<80) Moderate (50-80) Severe (30-50)	51 (29%) 95 (54%) 27 (16%)	12 (32%) 19 (61%) 6 (16%)	39 (29%) 76 (56%) 21 (15%)	0.904

IHD	Yes No	85 (13%) 585 (87%)	15 (17%) 73 (83%)	70 (12%) 512 (88%)	0.665
HTN	Yes No	279 (42%) 391 (58%)	37 (42%) 51 (58%)	242 (42%) 340 (58%)	0.934
Diabetes	Yes No	80 (12%) 590 (88%)	14 (16%) 74 (84%)	66 (11%) 516 (89%)	0.220
Smoking status	Current Ex Never	149 (22%) 391 (68.5%) 129 (22.5%)	35 (40%) 48 (54%) 5 (6%)	114 (20%) 343 (59%) 124 (21%)	<0.001

178 PPC, postoperative pulmonary complication; FEV_1, forced vital capacity in 1 second;
179 BMI, body mass index; ASA, American College of Anaesthetists; VATS, Video-assisted
180 thoracoscopic surgery; PCA, patient controlled analgesia; COPD, chronic obstructive
181 pulmonary disease; HTN, hypertension; IHD, ischaemic heart disease, NSLC, non-
182 small cell lung cancer.

183

184 Using backward logistic regression to identify perioperative variables independently
185 associated with PPCs our multivariate analysis included all variables. No significant
186 interactions across any of the variables were found. Only COPD diagnosis and
187 smoking status were associated with the development of a PPC (table 2). Patients
188 who had COPD were 1.81 times more likely to develop PPC compared to non-COPD
189 patients (95%CI 1.11–2.95; p=0.017). Current smokers were 5.42 times more likely to
190 develop PPC that never smokers (95%CI 1.99-14.76; p<0.001), and ex-smokers were
191 2.8 times more likely to develop PPC than never smokers (95%CI 1.08-7.28; p=0.035).

The goodness-of-fit test of this model remained non-significant during these steps with a p value very close to 1 showing a very good model fit (Hosmer and Lemeshow p=0.975). The overall predictive power of the model was 66.3% indicated by the area under the curve (ROC). The resulting logistic model had a sensitivity of 60.2% and specificity of 65.9% with the cut-off probability point set at 0.12. So in our model, a probability more than 0.12 means that a patients has 60.2% possibility to have a PPC. When the yielded probability is less than 0.12, patients have 65.9% chance to not develop PPC. The sensitivity of the model is the percentage of the group accurately identified by the model as having a PPC and the specificity is the percentage correctly identified as not having one.

Table 2 Preoperative risk factors associated with PPC on multivariate analysis.

Variables	**Estimate**	**SE**	**P-value**	**OR**	**95% CI**
Constant	-3.18	0.45	<0.001	-	-
COPD	0.59	0.25	0.017	1.81	1.11 - 2.95
Current smoker (vs. never)	1.69	0.51	<0.001	5.42	1.99 - 14.76
Ex smoker (vs. never)	1.03	0.49	0.035	2.80	1.08 - 7.28

COPD, chronic obstructive pulmonary disease.

Patients in the PPC group had a significantly longer (days) hospital LOS (12.7, 95%CI 10.5-14.9 vs. 6.3, 95%CI 5.9-6.7; p<0.001), longer HDU LOS (4.2, 95%CI 3.4-4.9 vs. 1.9 95%CI 1.8-2.1, p<0.001) and longer ITU LOS (2.1, 95%CI 1.0-3.3 vs. 0.2, 95%CI 0.1-0.4,

p<0.001). In the PPC group there were higher rates of ITU admissions (28% vs. 1.9%; p<0.001) (figure 1, table 3). The 30-day hospital readmission was higher in the PPC group (21% vs. 12%; p=0.023). Patients who developed a PPC in hospital had higher rate of readmission secondary to pneumonia and lower respiratory tract infections (9.1% vs. 3.8%; p=0.046).

Of all patients there were 176 (26%) deaths with a median follow up of 12 months (95%CI 9.4-14.6). Causes of death included early postoperative complications (8.5%), cancer related deaths (65%), non-cancer related deaths (21%) and cause of death uncertain (5%). Patients with a PPC had a significantly higher 30-day (9% vs. 0.7%; p<0.001) and 90-day mortality (17% vs. 2.9%; p<0.001).

Table 3 Morbidity and mortality following the development of a PPC.

Variables		**PPC (n=88)**	**Non-PPC (n=582)**	**P-value**
Number of ITU admissions		25 (28%)	11 (1.9%)	<0.001
Mean LOS (95% CI) (days)	Hospital	12.7 (10.5-14.9)	6.3 (5.9-6.7)	<0.001
	HDU	4.2 (3.4-4.9)	1.9 (1.8-2.1)	<0.001
	ITU	2.1 (1.0-3.3)	0.2 (0.1-0.4)	<0.001
Number of 30-day hospital readmissions	Total	18 (21%)	67 (12%)	0.023
	Pneumonia/LRTI	8 (9%)	22 (4%)	0.046
	Postoperative complication	10 (11%)	43 (7%)	0.198
	Uncertain	0	2 (0.3%)	0.754

Number of deaths	Total		37 (42%)	139 (24%)	<0.001
	30 day-mortality		8 (9%)	4 (0.7%)	<0.001
	90 day-mortality		15 (17%)	16 (3%)	<0.001
Cause of death	Postoperative complication		9 (10%)	6 (1%)	<0.001
	Excluding postoperative complication		28 (32%)	133 (22%)	0.017
	Cancer related		18 (20%)	97 (17%)	0.380
	Non-cancer related	Total	10 (11%)	27 (5%)	0.020
		Respiratory	6 (6.8%)	13 (2.2%)	0.028
		Cardiovascular	3 (3.4%)	10 (1.7%)	0.395
		Other	1 (1.1%)	4 (0.7%)	0.507
	Uncertain		0	9 (1.5%)	0.615

PPC, postoperative pulmonary complication; ITU, intensive treatment unit; LOS, length of stay; HDU, high dependency unit; LRTI, lower respiratory tract infection.

Excluding patients who died of a postoperative complication (15/670, 2%), those who develop a PPC have a reduced OS with a mean follow up of 40 months (95%CI 34.1-43.8 vs. 45.8, 95%CI 44.3-47.3; p=0.006) (figure 2). There were a significantly increased number of non-cancer related deaths in those who develop PPC (11 vs. 5%; p=0.020), of which, non-cancer respiratory cause of death are more frequent in patients with a PPC. Significant independent risk factors for late deaths in patients with NSCLC were PPC (Cox regression: HR 2.00, 95%CI 1.19-3.20; p=0.005), cancer stage, age and 30-day readmission to hospital (table 4).

232

233 **Table 4** Significant Independent risk factors for late deaths in patients with non-small

234 cell lung cancer.

Variables	Estimate	SE	P-value	HR	95% CI
PPC	0.69	0.25	0.006	2.00	1.19 – 3.20
Staging IIA/B	1.07	0.22	<0.001	2.92	1.89 – 4.56
Staging IIIA	1.28	0.25	<0.001	3.60	2.20 – 5.85
Staging IIIB	1.91	0.61	0.002	6.72	1.61 –18.90
Age	0.03	0.01	0.003	1.04	1.01 - 1.06
Readmission (30-days)	0.62	0.23	0.008	1.86	1.15- 2.89

235 PPC, Postoperative pulmonary complication.

236

237 **DISCUSSION**

238 Our study has confirmed that PPCs are common in thoracic surgery. The short-term
239 morbidity of developing a PPC following thoracic surgery is striking, with significantly
240 longer hospital, ITU and HDU LOS, higher frequency of ITU admissions and higher
241 frequency of hospital readmissions secondary to pulmonary infections. Furthermore,
242 patients who develop a PPC have a significantly increased mortality, both in the early
243 and late stages following surgery. After excluding immediate post-operative deaths,
244 developing a PPC is a significant independent risk factor for late deaths and these
245 patients have a worse long-term survival. Furthermore we observed a high rate of
246 non-cancer related deaths in this cohort.

247 The frequency of PPCs observed at this regional thoracic surgery unit (13%) is

concurrent with other studies [10-15]. The incidence of PPC following thoracic surgery ranges between studies predominantly because there is no standard; it is dependent on the type of complications included, the definition of pulmonary complications, and the type of surgery. Use of the objective MGS to define PPC does not include rare but serious postoperative complications such as broncho-pleural fistulas, which required re-operation in 0.4% of our patients, and also pulmonary embolism, which has been described in 2% of patients after thoracic surgery [16]. However, the fact that those more frequent, and probably less severe PPCs detected by the MGS were still associated with a higher short and long-term mortality rate is an important message.

Patients who develop a PPC are more than twice as likely to be readmitted within 30-days of surgery, and nearly 3 times more likely to re-present with respiratory tract infections. Hospital readmission is not only a serious morbidity; we demonstrate it also to be an independent risk factor for the late deaths observed in our study. Patients who are readmitted within 30-days of lung cancer surgery have been shown to have a 6-fold increase in 90-day postoperative mortality [17]. In our study the 90-day mortality was 2.6 times that of 30-day mortality, compatible with other study findings [9, 18]. Thus, this increased mortality following thoracic surgery is not explained by immediate postoperative deaths alone; we hypothesised that PPCs have a role in these later deaths observed.

Our study has shown that PPCs are significantly associated with reduced OS following thoracic surgery for lung resection. There is a paucity of data on the impact of PPCs on long-term outcome in thoracic surgery. A retrospective study

271 which included patients aged 66-80 who have undergone a lobectomy for stage 1
272 NSCLC found that development of a PPC was associated with reduced 5-year OS
273 (52.7 vs. 65.9%, p<0.001) and was an independent risk factor for mortality (HR 1.46,
274 95% CI, 1.24-1.73) [19]. We have also shown that developing a PPC is a independent
275 risk factor for late deaths, but in comparison our study is not limited by any inclusion
276 criteria other than national guidelines [6]. Therefore we have included those patients
277 who are older and have more advanced staging of cancer, which we and other
278 authors have found to be additional independent risk factors for late deaths [20, 21].

279 We demonstrate for the first time that after excluding immediate postoperative
280 deaths, patients with a PPC are more likely to die of late non-cancer related deaths.
281 This compares to the outcome of patients who are admitted to hospital secondary to
282 community acquired pneumonia (CAP), these patients have an increased risk of
283 subsequent pneumonia and mortality after discharge, and a substantial proportion
284 of these deaths are due to non-malignant respiratory disease [22]. Some of the late
285 deaths in patients who developed a PPC were secondary to cardiovascular disease,
286 indeed there is increasing evidence that pneumonia is associated with increased risk
287 of cardiovascular complications, which may be due to residual inflammation having a
288 role in triggering procoagulant pathways in these individuals [23].

289 COPD and current smoking were found to be independent risk factors in the
290 development of PPCs in ours and other studies [10, 21]. Our multivariate model for
291 assessing of risk factors has a c-index of 0.66 therefore it cannot be used as a
292 diagnostic/highly predictive tool as we would like a predictive power ideally more
293 than 80-90%. Nevertheless, our analysis identified factors having significant

association with PPC. Those patients diagnosed with COPD have increased risk of both pneumonia and atelectasis after surgery [24, 25]. We found on univariate analysis that a lower preoperative FEV_1 percentage predicted was associated with the development of a PPC, though on multivariate analysis, FEV_1 is not an independent risk factor, as previously shown [10]. In our study carbon monoxide lung diffusion capacity (DLCO) was performed only in patients with limited exercise tolerance or lung volumes so data are limited. However, studies have shown DLCO not to be an independent risk factor for long-term survival following thoracic surgery for lung cancer [26, 27]. Risk modification for patients with COPD would be through a pulmonary rehabilitation programme [28], which in thoracic surgery has shown encouraging results in reducing PPCs [29], but more robust studies are needed in this field.

Smoking is the biggest independent risk factor for developing PPCs; indeed our study has shown PPCs to be up to five times more common in current smokers when compared to never smokers, similar to other study findings [30]. Key mechanisms are likely to involve the effect smoking has on impairing the mucociliary escalator [31], and also both the antimicrobial and pro-inflammatory functions of alveolar macrophages, which decreases further during anaesthesia and surgery [32]. Risk modification would be in the form of smoking cessation; however the duration needed in order to reduce postoperative risk remains a debated topic and is a much-needed area of future research.

Independent risk factors for developing PPCs have previously been identified as smoking, advanced age (≥75 year old), reduced mobility, ASA ≥3, cardiovascular

comorbidity, COPD and BMI >/ 30kg/m^2 [10-14]. Interestingly BMI, age and ASA were not significant risk factors for the development of PPCs in our study. Other investigators have found that obesity does not confer greater morbidity and mortality after lung resection [33]. We have shown that age is not a predictive factor for development of PPC which we believe is an important finding for the clinical community and is supported by other studies showing no significant difference in postoperative complications in patients over the age of 75 [21, 34].

Study strengths and limitations

This is a real-life study involving consecutive patients undergoing thoracic surgery in a tertiary centre; our patient demographics and staging of cancer is comparable to national data [9]. The main limitation of our study is the low number of VATS cases recorded. VATS lobectomy has since increased to 1/3 of all lobectomies carried out in the UK due to the perceived minimally invasive nature of the procedure with reduced complications. Indeed we have previously described that the PPC incidence in VATS cases seems to be lower [35]. The data of this study precedes the growth of VATS lobectomies, therefore the majority of our lung resections over the time frame were done via thoracotomy, within in the latter half of the study 2 of the 5 surgeons had started to perform an increasing number of VATS lobectomies (35%), compared to the first half of the study period (3.4%). The finding of VATS approach not to show a significant reduction in incidence of PPC is most likely because of under powering. Further studies into the effects of transition of thoracotomy to VATS on PPC frequency and long-term outcome will need to be conducted. There is limitation with regards to the patient follow up data; as information on mortality and cause of

death were obtained from hospital records and death certificates in a retrospective manner, in a few patients cause of death could not be ascertained (5%). Additionally, we did not follow up for cancer recurrence and therefore could not assess the effect of PPC on disease free survival in patients with lung cancer, which would be an interesting area for further investigation.

CONCLUSION

In summary, developing a PPC after thoracic surgery is associated with a poorer long-term outcome. We have found COPD and smoking are independent risk factors for developing PPCs, whilst age was not a predictive factor. Further research is required into the effect of risk modification on the development of PPCs and subsequent long-term outcome following thoracic surgery.

Contributors

STL carried out data collection and drafted the final manuscript. PJA, AK, KA carried out data collection. TT performed the statistical analysis. EB, MSK, PBR, RSS and BN were involved in patient selection for surgery. BN and DRT have critically reviewed the manuscript and given final approval of the version to be published. All authors read and approved the final manuscript.

Competing interests

There are no conflicts of interests to declare.

Ethics approval

The study received ethics approval by the National Research Ethics Service (NRES) Committee West Midlands, Edgbaston.

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FIGURE LEGENDS

Figure 1 Effect of PPC on hospital length of stay (days). PPC, postoperative pulmonary complication; LOS, Length of stay; ITU, Intensive treatment unit; HDU High dependency unit, TOTAL; Total length of hospital stay.

Figure 2 Overall survival of patients with and without a PPC excluding early postoperative deaths. PPC, Postoperative pulmonary complication; Black line: no PPC, Grey line: PPC.